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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/722,661	11/24/2003	Anton Berns	8535-068-999	7750

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EXAMINER	
CHEN, SHIN LIN	
ART UNIT	**PAPER NUMBER**
1632	
MAIL DATE	**DELIVERY MODE**
10/03/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	Application No.	Applicant(s)	
	10/722,661	BERNS ET AL.	
	Examiner	Art Unit	
	Shin-Lin Chen	1632	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 22 August 2007 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____ months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☒ The Notice of Appeal was filed on *02 August 2007*. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☒ Applicant's reply has overcome the following rejection(s): 35 U.S.C. 112 second paragraph and 35 U.S.C. 112 first paragraph.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: *None*.
   Claim(s) objected to: *None*.
   Claim(s) rejected: *89-98 and 100-127*.
   Claim(s) withdrawn from consideration: *99*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

Shin-Lin Chen
Primary Examiner
Art Unit: 1632

Continuation of 11. does NOT place the application in condition for allowance because: Applicants argue that Capecchi's statement "experimenter chooses both which gene to mutate and how to mutate" says nothing about the genomic DNA flanking the gene to be mutated, and the statement "knowledge generated within the species or from other species" only applies to selecting which target gene to mutate. Capecchi does not teach using a single inbred strain of animal as the source of both flanking sequence of the targeting DNA construct and the targeted cells (amendment, p. 9). This is not found persuasive because of the reasons of record. Both of Capecchi's statements do imply how to use the flanking sequence of the targeting DNA construct. Capecchi teaches that "the application of this approach to mouse genetics is dependent on the availability of a cloned, genomic fragment of the chosen locus. At present this does not appear to be a limitation. The number of abailable cloned mouse genes that now exist is very large and new methods for isolating additional genes are continually being developed" (e.g. p. 70, right column). Capecchi also teaches that "the frequency of recombinantion between co-introduced DNA molecules is strongly proportional to the extent of homology between them. When DNA molecules share more than 5 kilobases of homology, then nealy every molecule introduced into cell nucleus participates in at least one recombination event" (e.g. p. 71, left column, top paragraph). Thus, the teachings "which gene to mutate and how to mutate" and "knowledge generated within the species or from other species" imply requirement of the availability of a cloned genomic fragment of the chosen locus, i.e. the knowledge of the flanking sequence of the targeting DNA construct. It would be preferred that the flanking sequence and the sequence at the genome of the targeted cells are the same, i.e. they are from the same inbred strain of animal, because Capecchi teaches that "the frequency of recombinantion between co-introduced DNA molecules is strongly proportional to the extent of homology between them". Further, the term "homologous recombination" means that the sequences recombine to each other have very high homology, and the higher the homology the merrier, i.e. 100% homology would be preferred. Thus, the teachings of Capecchi encompass the use of a single inbred strain of animal as the source of both the flanking sequences of the targeting DNA construct and the targeted cells. Applicants cite page 70, right column, 2nd paragraph of Capecchi and argue that Capecchi does not concern the genetic background of the genome of the embryonic stem cell. Applicants further cite delcaration by Dr. Anton Berns and argue that at the time of the invention, most of the mouse genomic libraries used for making the targeting DNA construct were derived from BALB/c or Black 6 mouse strains, and there were numerous requests for the mouse strain 129 genomic library constructed by Dr. Berns. Capecchi does not teach using same genetic background of inbred strain of animal as the source of the flanking sequence and the targeted ES cell (amendment, p. 9-10). This is not found persuasive because of the reasons of record and the reasons set forth above, and the following reasons. Firstly, the claims do NOT recite the inbred strain of animal has to be mouse strain 129. Secondly, since there were numerous requests for the mouse strain 129 genomic library it is evidenced that one of ordinary skill in the art at the time of the invention has already known to use the mouse strain 129 genomic library for preparing the targeting DNA construct. Thirdly, Capecchi teaches that "the application of this approach to mouse genetics is dependent on the availability of a cloned, genomic fragment of the chosen locus. At present this does not appear to be a limitation. The number of abailable cloned mouse genes that now exist is very large and new methods for isolating additional genes are continually being developed" (e.g. p. 70, right column). Capecchi shows that the technology for preparing genomic DNA library and isolation of genomic frament was known at the time of the invention and one of ordinary skill would know how to prepare and isolate genomnic clone from the mouse strain 129 genomic library. Request for the mouse strain 129 genomic library constructed by Dr. Berns does not mean that one of ordinary skill in the art at the time of the invention does not know how to prepare mouse strain 129 genomic library and how to isolate genomic clone from said library. Applicants argue that, according to case law, the fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that reuslt or characteristic. the teahcings of Capecchi do not rise to the level of inherent anticipation that both the flanking sequence and the target cells come from the same inbred strain of mice (amendment, p. 10). This is not found persuasive because of the reasons of record and the reasons set forth above. Applicants argue that the cited '764 patent" is not a reference under 35 U.S.C. 102(b) because the present applciation has priority date of 8-20-91 and the '764 patent" was issued on 11-7-95. The term "102(b)" on page 6, line 1 of Official action mailed 5-11-07 is a typographical error. The term "102(b)" should be "102(e)" (please see page 8, line 1 of Official action mailed 8-22-06). The effective filing date of "764 ptaent" is 8-22-89. Applicants argue that '764 patent does not teach every element of the claimed invention and '764 patent teaches using targeting DNA (mouse ARK cell line) and target DNA (C57BL/6 or CC1.2) from different sources (amendment, p. 11). This is not found persuasive because of the reasons of record and the reasons set forth above. '764 patent teaches a method for producing an alteration in a gene of interest by targeting through homologous recombination via the use of mouse ES cells. '764 patent teaches using a vector comprising a first DNA sequence substantially homologous to a portion of a first region of a target DNA sequence and a second DNA sequence substantially homologous to another portion of a second region of a target DNA sequence (column 5, lines 1-12). The term "substantially homologous" means that the sequences recombine to each other have very high homology, and the higher the homology the merrier, i.e. 100% homology would be preferred. The teaching of '764 patent encompasses using targeting DNA sequence and the target DNA sequence both from the same source, i.e. from same mouse strain. thus, the claims remain rejected for the reasons of record and the reasons set forth above .